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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,424	04/19/2007	Mario Contorni	PAT051830-US-PCT	7898

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EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,424	CONTORNI, MARIO	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,9-14 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,9-14 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment filed February 9, 2010 has been received and entered. Claims 4, 7-8, 15-16 and 18-20 have been cancelled. Accordingly, claims 1-3, 5-6, 9-14, and 17 are pending in the instant application.

Claim Objections

1. The objection of claims 5-15 and 17 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend upon a multiple dependent claim is withdrawn in view of Applicants amendment.

Claim Rejections - 35 USC § 101

2. The rejection of claim 16 for the use of the composition, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass is withdrawn in view of the cancellation of said claim.

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-3 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, a written description rejection is maintained. Additionally in view of Applicants amendment, this rejection is

applied to claims 5-6, 9-14 and 17.

Applicants are asserting that claim 1 has been amended to specify five specific serogroup B antigens, and that the five antigens are defined by reference to specific sequences.

Applicants arguments have been fully considered but are not found to be persuasive.

Applicants have amended claim 1 to recite “50% or more identity to SEQ ID NO: 2, 3, 4, 5, and 6."

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, “50% identical and able to induce an immune response that is bactericidial” alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

Applicants are directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, the guidelines can be found at the following link on the USPTO Internet in "Patents Guidance" Specifically, Example 11, which is analogous to the recitation of 50%

identity and having a particular function (able to induce an immune response that is bactericidal).

<http://www.uspto.gov/web/patents/guides.htm>

4. The rejection of claims 1-3 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Additionally in view of Applicants amendment this rejection is newly applied to claims 5-6, 9-14 and 17.

Applicants are asserting that claim 1 has been amended to specify five specific serogroup B antigens, and that the five antigens are defined by reference to specific sequences.

Applicants arguments have been fully considered but are not found to be persuasive.

Applicants have amended claim 1 to recite "50% or more identity to SEQ ID NO: 2, 3, 4, 5, and 6, as well as any 7 or greater consecutive amino acids from these sequences.

The following new references are applied in view of Applicants amendment:

Salgaller et al (Cancer Immunol Immunother. Vol. 39, pp 105-116, 1994) teach that in patients with melanoma, cytolysis of target cells pulsed with the synthetic MAGE-1 decapeptide KEADOTGHSY was superior to that of cells pulsed with the

immunodominant nonapeptide. Single amino-acid or even side chain substitutions in the immunodominant nonamer abrogated cytolysis. The cytotoxic T lymphocyte (CTL) lysed target cells expressing the MAGE-1 nonapeptide, including established tumor cell lines, and immortalized EBV-B lines pulsed with peptide. Yet it did not lyse targets pulsed with a peptide containing amino acid substitutions of the natural nonamer. Thus single amino-acid deletions or substitutions have been shown to reduce recognition by CTL. This reference demonstrates that even a single amino acid substitution, deletion or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein.

Fox (U.S. Patent Number 4,879,213) sets forth that "without knowing a protein's three dimensional structure there is no reliable method for determining which linear segments of the protein are accessible to the host's immune system" and that "whether the three dimensional structure is known or not, short linear polypeptides often appear not to have the ability to mimic the required secondary and tertiary conformational structures to constitute appropriate immunogenic and antigenic determinants." (See column 3)

Applicants SEQ ID NO: 1 contains 350 amino acids. 50% substitution would allow for 175 amino acids to be substituted. Expressed mathematically that is $(20)^{175}$ possible combinations. Doing the math that equals 4.78×10^{227}, a number the Examiner cannot even comprehend or for that matter name.

Concerning the Wands analysis, Applicant's specification provides no guidance or working examples as to which of the plethora of "50% variants, or short peptides" of

SEQ ID NO: 1-6 are useful for inducing a bactericidal response, with the exception of those specifically identified by the full length SEQ ID NO: 1-6. (Factors II and III). Furthermore, as shown in the art by Fox and Salgaller et al, altered proteins, and protein fragments are frequently not capable of binding the same molecules as the full length unmodified protein. Consequently one of skill in the art would be forced into excessive experimentation to identify which "50% variants or 7 or more consecutive amino acid" molecules are capable of inducing a bactericidal response.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

First, as set forth by Plotkin et al (VACCINES W.B. Saunders Company, 1988, page 571) "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies… and thus protect the host against attack by the pathogen." This

teaching directly addresses factors 1, 4, 5, 6, 7 and 8.

Second, Cripps et al (Current Opinion in Immunology Vol. 14, pp 553-557, 2002) teach of obstacles of nonpolysaccharide antigens for N. meningitidis including a "diverse repertoire" of variability. (See page 555). Cripps et al further set forth that high-thoroughput genomic analysis may speed up the identification of potential vaccine antigens, however this approach does not allow prediction of surface expression or which sequence the microbe is using. Cripps et al conclude that "testing the ***plethora of proteins***" produced in this way in animal systems will be the rate limiting step to further advancement. (Emphasis added; see page 556).

A vaccine/bactericidial "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d 1557,1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Given the lack of guidance, lack of a clear structure set forth in the claims, and the unpredictable nature of the invention, one of skill in the art would be forced into excessive experimentation in order to practice the instantly claimed invention.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

Claim Rejections - 35 USC § 103

5. The rejectin of claims 18-20 under 35 U.S.C. 103(a) as being unpatentable over Ryall in view of Boutriau et al is withdrawn in view of the cancellation of said claims.

The following new grounds of rejection are applied to the amended claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-3, 5-6, 9-13, and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Constantino (US Publication 2007/0082014).

Constantino disclose of conjugated serogroup C capsular saccharide antigens, conjugated serogroup W 135 antigens, conjugated serogroup Y antigens, conjugated serogroup A antigens, and serogroup B antigens. (See claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3, 5-6, 9-14, and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-63 of copending Application No. 10/543,455. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims encompasses conjugated serogroup C capsular saccharide antigens, conjugated serogroup W 135 antigens, conjugated serogroup Y antigens, conjugated serogroup A antigens, and serogroup B antigens (741, 936, 953 and 287 proteins; see claim 44).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Specification

8. The amendment filed February 9, 2010 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

"The teachings of the above applications are incorporated herein in their entirety by reference." Incorporation by reference can only be done at the time of filing, any attempt to later incorporate by reference is not permitted.

Applicant is required to cancel the new matter in the reply to this Office Action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Navarro/
Primary Examiner, Art Unit 1645
April 10, 2010